

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:

1340-1-034N(SJ-0029)

Inventors:

Schuetz et al.

Serial No.:

09/974,619

Filing Date:

October 10, 2001

Examiner:

Johannsen, Diana B.

Group Art Unit:

1634

Title:

Genotyping Assay to Predict CYP3A5

Phenotype

"Express Mail" Label No. EV331020856US Date of Deposit - October 7, 2003

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Mail Stop Sequence Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

Amendment in Response to Notice to Comply

Please enter the following amendments and remarks into the record.

Amendments to the Specification begin at page 2.

Remarks begin at page 5.

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Table 4 * CYP3A5 alleles

1 18826 15983 catacagactate (SEO ID NO-42) catacaggacagtat (SEO ID NO-42) catacaggacagtat (SEO ID NO-43) catacaggacagtat (SEO ID NO-44) catacaggacagtat (SEO ID NO-45) catacaggacatat (SEO ID NO-45) catacaggacagtat (SEO ID NO-45) catacaggacagta	CYP3A5	exon	starts in AC005020*	ends in AC005020	5' splice site	3' splice site	functional consequence
2 19601 19694 ctttgragatarigg (SEO ID NO:42) 3 21224 21276 tctcccagggtct (SEO ID NO:44) 4 22894 23025 tctttca[A/G]atctc (SEO ID NO:46) 4 23130 23229 ccacacagaacgta (SEQ ID NO:48) 5 28744 28857 aatcgtagatttg (SEQ ID NO:50) 6 29120 29096 atgtacagaaaga (SEQ ID NO:50) 7 30495 30643 ccactcagcatctt (SEQ ID NO:58) 8 31714 31841 tcccacagaactt (SEO ID NO:60)		1	15826	15983		ctatctgtgagtaa (SEQ ID NO:41)	
3 21224 21276 tctcccagggtctc (SEO ID NO:44) 4 23130 23229 tctttcd A/G]tatctc 5 28744 24036 attcgtagattgt (SEO ID NO:50) 6 29120 29208 gtgcttagatgtt (SEO ID NO:54) 7 30495 30643 ccactcagaactt (SEO ID NO:56) 8 31714 31841 tcccacagactt (SEO ID NO:58)		2	19601	19694	ctttgtagatatgg (SEQ ID NO:42)	cgtcaaggtgagtta (SEO ID NO:43)	
4 23130 23229 ccacacagaacgta (SEQ ID NO:48) 4 23130 23229 ccacacagaacgta (SEQ ID NO:48) 5 28744 28857 aactctagtcttt (SEQ ID NO:50) 6 28999 29096 atgtacagaaaga (SEQ ID NO:54) 7 30495 29208 gtgcttagatgtt (SEQ ID NO:56) 8 31714 31841 tcccacagaactt (SEQ ID NO:60)		3	21224	21276	teteccagggtete (SEQ ID NO:44)	gtggggggggagtat (SEQ ID NO:45)	
4 23130 23229 ccacacagaacgta (SEQ ID NO:48) 5 28744 28857 aactctagtcttt (SEQ ID NO:52) 6 29120 29096 atgtacagaaaga (SEQ ID NO:54) 7 30495 30643 ccactcagcatctt (SEQ ID NO:58) 8 31714 31841 tcccacagaactct (SEQ ID NO:60)	3B, insertion from intron 3		22894	23025	tettea[A/G]tatete (SEQ ID NO:46)	ciaggggatggat (SEQ ID NO:47)	CYP3AS*3-22893G; insertion of exon 3B into SV1, SV2, SV3; premature stop after aminoacid 102
5 28744 28857 aactctagtcttt (SEO ID NO:52) 6 28999 29096 atgtacagaaaga (SEO ID NO:54) 7 30495 29208 gtgcttagatgttc (SEO ID NO:56) 8 31714 31841 tcccacagactct (SEO ID NO:60)		4	23130	23229	ccacacagaacgta (SEQ ID NO:48)	cgaagggtaagcat (SEO ID NO:49)	
s 2874 28857 aactctagtcttt (SEQ ID NO:52) rtion from 28999 29096 atgtacagaaaga (SEQ ID NO:54) 6 29120 29208 gtgcttagatgttc (SEQ ID NO:56) 7 30495 30643 ccactcagcatctt (SEQ ID NO:58) 8 31714 31841 tccacagaactct (SEQ ID NO:60)	4B, insertion from intron 4		23931	24036	attegtagattigt (SEQ ID NO:50)	g[A/G]caggttct (SEQ ID NO:51)	CYP3A5*3-insertions of exon 4B into SV2 and SV3
rion from 28999 29096 atgtacagaaaaga (SEQ ID NO:54) 6 29120 29208 gtgcttagatgttc (SEQ ID NO:56) 7 30495 30643 ccactcagcatctt (SEQ ID NO:58) 8 31714 31841 tcccacagtactct (SEQ ID NO:60)		80	28744	28857	aactctagtcttt (SEQ ID NO:52)	aaggaggtatgaaa (SEQ ID NO:53)	
29120 29208 grgcttagatgtt (SEQ ID NO:56) 30495 30643 ccactcagcatctt (SEQ ID NO:58) 31714 31841 tcccacagactct (SEQ ID NO:60)	5B, insertion from intron 5		28999	29096	atgracagaaaga (SEO ID NO:54)	ctacaggtactgat (SEQ ID NO:55)	CYP3A5 *3-insertion of exon 5B into SV3
30495 30643 ccactcagcatctt (SEQ ID NO:58) 31714 31841 tcccacagtactct (SEQ ID NO:60)		9	29120	29208	grgcttagatgrtc (SEQ ID NO:56)	gaaagagtaagtag (SEO ID NO:57)	CYP3A5*3-deletion of exon 6 from SV3
31714 31841 tcccacagtactct (SEQ ID NO:60)		7	30495	30643	ccactcagcatctt (SEQ ID NO:58)	caataagtatgtgg (SEQ ID NO:59)	CYP3A5*6-30597G>A; deletion of exon 7 from splice variant; frame shift and premature stop at 184 aa
The same of the sa		8	31714	31841	tcccacagtactct (SEQ ID NO:60)	caaaaggtaaaatc (SEQ ID NO:61)	de de la companya de

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CYP3A5	ехоп	starts in AC005020*	ends in AC005020	5' splice site	3' splice site	functional consequence
	6	32927	32993	gcttctagcaccga (SEO ID NO:62)	acaaaggtaaccaa (SEO ID NO:63)	
	10	35150	35310	cettteagetetgt (SEQ ID NO:64)	aataaggtgaggg (SEO ID NO:65)	
	111	43030	43256	cttccaggcacca (SEQ ID NO:66)	tgaaaggtacaagt (SEO ID NO:67)	
	12	45577	45736	ggaactaggttcag (SEO ID NO:68)	acacaggtcagtac (SEQ ID NO:69)	
	13	47409	47615	tattgtagatccc (SEQ ID NO:70)		

*The accession numbers for the reference CYP3A5*1cDNA and CYP3A5*3 are J04813 and AC005020, respectively. SV1, splice variant-1; SV2, mRNA. CYP3A5*1 contains an A at nt 22,893 generating a sequence of [tttcAAtatc] and no aberrant splicing of CYP3A5 mRNA. To renumber the mutation sites according to the translation start site (nt 15913 is A in ATG initiation codon) subtract 15912 bases from the SNP location (e.g.; splice variant-2; SV3, splice variant -3. CYP3A5*3 has a G at nt 22,893 and a consensus splice of [tttcAGtatc] and aberrant splicing of CYP3A5 the location of CYP3A5*6 is 14685G>A). Incom.







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Alexandria VA 22313-1450.

Typed Name: Kathleen A. Tyrrell, Reg. No. 38,350

Mail Stop Sequence Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

RESPONSE TO NOTICE TO COMPLY

In response to the "Notice to Comply" dated September 9, 2003, a response to which is due October 9, 2003, enclosed herewith is:

- (XX) Amendment in Response to Notice to Comply;
- Submission Support Filing and (XX) Statement to Accordance with 37 CFR §§1.821 through 1.825;

- (XX) Substitute pages of the Sequence Listing;
- (XX) Substitute copy of the computer readable form of Sequence Listing;
- (XX) Copy of Notice to Comply;
- () Petition for Three (3) Month Extension of Time;
- () Other: _____.

The Commissioner is hereby authorized to charge any underpayment associated with this communication or credit any overpayment to Deposit Account No. 50-1619. This sheet is attached in duplicate.

Respectfully submitted,

Kathleen A. Tyrell

Registration No. 38,350

Date: October 7, 2003

Licata & Tyrrell P.C. 66 E. Main Street Marlton, New Jersey 08053

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